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5,5'-Arylmethylenebis(2-amino-4,6-dihydroxypyrimidines)

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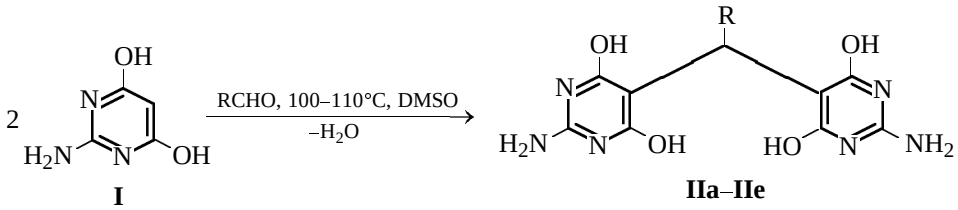
Abstract — Condensation of 2-amino-4,6-dihydroxypyrimidine with aromatic aldehydes at 100–110°C in DMSO gave a series of 5,5'-arylmethylenebis(2-amino-4,6-dihydroxypyrimidines).

We previously reported on the synthesis of a large series of 5,5'-ylidenebis(4,6-dihydroxypyrimidines) and some their 2-methyl and 2-methylthio derivatives [1–3]. The main approach to such compounds is based on the condensation of the corresponding hydroxypyrimidines with aldehydes. From 2-amino-4,6-dihydroxypyrimidine we succeeded in obtaining only 5,5'-(4-nitrobenzylidene)bis(2-amino-4,6-dihydroxypyrimidine) [3]. The reactions were carried out in boiling pyridine.

The present communication describes the synthesis of a series of 5,5'-arylmethylenebis(2-amino-4,6-dihydroxypyrimidines) **II** by reaction of 2-amino-4,6-dihydroxypyrimidine (**I**) with aromatic aldehydes according to the following scheme:



I **IIa**–**IIe**

X = NH_2, R = $C_6H_4NO_2$-4 (**a**), C_6H_4OH-3 (**b**), $C_6H_4NMe_2$-4 (**c**), C_6H_4OMe-4 (**d**), $C_6H_3(OMe)_2$-2,4 (**e**).

2-Amino-4,6-dihydroxypyrimidine (**I**) turned out to be less reactive than 2-unsubstituted, 2-methyl, and 2-methylthio analogs. Therefore, the reactions with aminopyrimidine **I** were performed at 100–110°C and in a more polar solvent than pyridine, namely in DMSO. The yields of the final products were 60–100%. Compounds **II** are yellowish finely crystalline powders which are almost insoluble in water and in most organic solvents (except for DMSO). They have no sharp melting points and decompose on heating above 300°C. The purity and structure of the products were proved by TLC, elemental analysis, and ^1H and ^{13}C NMR, IR, and UV spectroscopy. The NMR spectra were the most informative.

In the ^1H NMR spectra of compounds **IIa**–**IIe** we observed signals from one CH proton in the region δ 5.8–6.0 ppm, four amino group protons as a broadened singlet at δ 6.6–6.8 ppm, four NH and OH protons as a broadened singlet at δ 11–12 ppm, and aromatic protons at δ 6–8 ppm. The spectral pattern in the aromatic region depends on the position of substituents in the benzene ring. The ^{13}C NMR spectra of **IIa**–**IIe** contained signals from the methine carbon atom at δ_C 27–31 ppm, C^2 and C^5 of the pyrimidine ring at δ_C 150 and 93–94 ppm, respectively, a common signal from C^4 and C^6 (δ_C 165–166 ppm), and also signals from aromatic carbon atoms and substituents in the aromatic ring.

The IR spectra of the products support their structure. In particular, two bands in the region 3150–3400 cm^{-1} belong to stretching vibrations of N–H bonds in primary amino groups, and a broad composite band at 1600–1700 cm^{-1} arises from vibrations of the carbonyl groups, presumably belonging to different tautomers.

The UV spectra of **IIa**–**IIe** are characterized as a rule by the presence of two absorption maxima. One of these is located at λ 250–270 nm; it results

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from π,π^* transitions in the pyrimidine fragments. The position and intensity of the second maximum strongly depend on the substituent in the benzene ring. Obviously, the latter originates from π,π^* transitions in the aromatic electron system.

Thus we have found conditions for synthesis and proved the structure of a series of new compounds, 5,5'-arylmethylenebis(2-amino-4,6-dihydroxypyrimidine) derivatives.

EXPERIMENTAL

The IR spectra of samples dispersed in mineral oil were recorded on a Specord IR-75 spectrometer. The ^{1}H and ^{13}C NMR spectra of solutions in DMSO-d_6 were obtained on a Bruker AM-500 instrument at 500 and 75 MHz, respectively, using HMDS (^{1}H) and DMSO-d_6 (^{13}C) as reference. The UV spectra of ethanolic solutions (containing ~1 vol % of DMSO) or solutions in methanol were measured on an SF-56 spectrophotometer [concentration $(2–5)\times10^{-5}$ M]. TLC analysis was performed on Silufol UV-254 plates using ethyl acetate–acetic acid–methanol, (9 : 0.5 : 0.5) as eluent. 2-Amino-4,6-dihydroxypyrimidine and substituted benzaldehydes were commercial products.

5,5'-Arylmethylenebis(2-amino-4,6-dihydroxypyrimidines) IIa–IIe. A mixture of 0.01 mol of aminopyrimidine **I**, 0.005 mol of appropriate benzaldehyde, and 8–10 ml of DMSO was stirred for 20 min to 8 h (depending on the aldehyde nature) at 100–110°C. The mixture was cooled and diluted with water, and the precipitate was filtered off, heated for 30 min in boiling acetic acid to remove residual DMSO, filtered off again, washed with ethanol, and dried at 80°C.

5,5'-(4-Nitrobenzylidene)bis(2-amino-4,6-dihydroxypyrimidine) (IIa). Reaction time 20 min. Yield 98%. Decomposes above 350°C. IR spectrum, ν, cm^{-1}: 470, 545, 590, 630, 655, 690, 725, 775, 790, 850, 880, 1090, 1110, 1155, 1210, 1300, 1350, 1520 (NO_2), 1630 v.s, 1700 (C=O), 2720, 3200, 3340 (N–H). UV spectrum (EtOH), λ_{max}, nm ($\log\varepsilon$): 270 (4.43). ^{1}H NMR spectrum, δ, ppm: 6.10 s (1H, 5-CH), 6.83 br.s (4H, NH_2), 7.27 d (2H, H_{arom}, J = 8 Hz), 8.06 d (2H, H_{arom}, J = 8 Hz), 11.40 br.s (4H, NH, OH). ^{13}C NMR spectrum, δ_C, ppm: 31.67 (ArCH), 92.65 (C^5), 122.81 (C_{arom}), 127.76 (C_{arom}), 145.05 (C_{arom}), 152.05 (C_{arom}), 152.79 (C^2), 165.32 (C^4, C^6). Found, %: C 46.23; H 3.57; N 25.02. $C_{15}H_{13}N_7O_6$. Calculated, %: C 46.52; H 3.38; N 25.31.

5,5'-(3-Hydroxybenzylidene)bis(2-amino-4,6-dihydroxypyrimidine) (IIb). Reaction time 20 min. Yield 69%. Decomposes at 300–310°C. IR spectrum, ν, cm^{-1}: 470, 530, 545, 555, 580, 640, 650, 675, 695, 720, 770, 785, 800, 830, 920 br., 1065, 1090, 1130, 1175, 1275, 1620 v.s, 1710 (C=O), 2720, 3180, 3350 (N–H), 3610 (O–H). UV spectrum (EtOH), λ_{max}, nm ($\log\varepsilon$): 268 (4.09). ^{1}H NMR spectrum, δ, ppm: 5.90 s (1H, 5-CH), 6.47 m (3H, H_{arom}), 6.70 br.s (4H, NH_2), 6.93 m (1H, H_{arom}), 8.93 s (1H, OH), 10.90 br.s (4H, NH, OH). ^{13}C NMR spectrum, δ_C, ppm: 30.78 (ArCH), 93.47 (C^5), 111.58 (C_{arom}), 113.59 (C_{arom}), 117.35 (C_{arom}), 128.23 (C_{arom}), 144.62 (C_{arom}), 152.41 (C^2), 156.78 (C_{arom}), 165.72 (C^4, C^6). Found, %: C 50.12; H 4.18; N 23.14. $C_{15}H_{14}N_6O_5$. Calculated, %: C 50.28; H 3.94; N 23.45.

5,5'-(4-Dimethylaminobenzylidene)bis(2-amino-4,6-dihydroxypyrimidine) (IIc). Reaction time 8 h. Yield 73%. Decomposes above 370°C. IR spectrum, ν, cm^{-1}: 450, 485, 530, 555, 630, 660, 690, 725, 790, 825, 835, 880, 960, 995, 1030, 1100, 1200, 1220, 1270, 1520, 1550, 1625, 1675, 1700 v.s (C=O), 2720, 3160, 3330 (N–H). UV spectrum (EtOH), λ_{max}, nm ($\log\varepsilon$): 258 (4.36), 466 (4.35). ^{1}H NMR spectrum, δ, ppm: 2.80 s (6H, NMe_2), 5.83 s (1H, 5-CH), 6.56 d (2H, H_{arom}, J = 8 Hz), 6.65 br.s (4H, NH_2), 6.80 d (2H, H_{arom}, J = 8 Hz), 10.80 br.s (4H, NH, OH). Found, %: C 53.22; H 4.75; N 25. 31. $C_{17}H_{19}N_7O_4$. Calculated, %: C 52.98; H 4.97; N 25.44.

5,5'-(4-Methoxybenzylidene)bis(2-amino-4,6-dihydroxypyrimidine) (IId). Reaction time 2 h. Yield 61%. Decomposes at 315–320°C. IR spectrum, ν, cm^{-1}: 475, 545, 565, 600, 650, 680, 725, 765, 785, 805, 840, 860, 890, 920, 935, 1035, 1090, 1175, 1215, 1250, 1310, 1510, 1620 v.s (C=O), 2720, 3200, 3350 N–H). UV spectrum (EtOH), λ_{max}, nm ($\log\varepsilon$): 268 (4.19), 380 (3.34). ^{1}H NMR spectrum, δ, ppm: 3.68 s (3H, OMe), 5.88 s (1H, 5-CH), 6.65 br.s (4H, NH_2), 6.73 d (2H, H_{arom}, J = 8 Hz), 6.89 d (2H, H_{arom}, J = 8 Hz), 10.90 br.s (4H, NH, OH). ^{13}C NMR spectrum, δ_C, ppm: 30.10 (ArCH), 54.79 (OMe), 93.69 (C^5), 112.92 (C_{arom}), 126.86 (C_{arom}), 131.73 (C_{arom}), 152.46 (C^2), 156.60 (C_{arom}), 165.72 (C^4, C^6). Found, %: C 51.88; H 4.15; N 22.63. $C_{16}H_{16}N_6O_5$. Calculated, %: C 51.61: H 4.33; N 22.57.

5,5'-(2,4-Dimethoxybenzylidene)bis(2-amino-4,6-dihydroxypyrimidine) (IIe). Reaction time 2 h. Yield 75%. Decomposes above 350°C. IR spectrum, ν, cm^{-1}: 450, 480, 525, 540, 555, 570, 600, 630, 655, 680, 720, 780, 800, 815, 830, 845, 860, 905, 945, 960, 990, 1025, 1040, 1065, 1095, 1130, 1160, 1180, 1210, 1240, 1275, 1305, 1320, 1555, 1600, 1620, 1645, 1695 v.s, 1720 (C=O), 3170, 3330 (N–H). UV spectrum (EtOH), λ_{max}, nm ($\log\varepsilon$): 258 (4.25), 408 (3.98). ^{1}H NMR spectrum, δ, ppm: 3.56 s (3H,

OMe), 3.68 s (3H, OMe), 5.86 s (1H, 5-CH), 6.40 m (2H, H_{arom}), 6.55 br.s (4H, NH_2), 6.93 m (1H, H_{arom}), 10.80 br.s (4H, NH, OH). ^{13}C NMR spectrum, δ_C, ppm: 26.96 (ArCH), 54.86 (OMe), 55.38 (OMe), 93.88 (C^5), 98.36 (C_{arom}), 103.31 (C_{arom}), 124.00 (C_{arom}), 128.78 (C_{arom}), 152.20 (C^2), 157.75 (C_{arom}), 158.05 (C_{arom}), 165.70 (C^4, C^6). Found, %: C 50.92; H 4.69; N 20.49. $C_{17}H_{18}N_6O_6$. Calculated, %: C 50.75; H 4.51; N 20.89.

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